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No 17

# EARLY HUMAN EMBRYOS AND THE MODE OF THEIR PRESERVATION.

By FRANKLIN P. MALL,
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Nearly all human embryos which come into the possession of embryologists are of little value for careful study, because they have been preserved carelessly. Of fifty embryos less than six weeks old, which have come into the writer's hands during the last few years, only six have proved to be of value, and these came from three physicians. In nearly all cases the specimen is destroyed by placing the ovum in very dilute alcohol, and in so doing it is handled very roughly. Poor specimens, however, are better than none at all, therefore in all cases the ova should be preserved, even if there be but little hope to obtain a good specimen. *The best and most convenient method of preserving young embryos is to place the unopened ovum, with the least possible handling, in a large quantity of very strong alcohol.* The alcohol of druggists is in no case too strong, and, according to my experience, is as a rule too weak. Often the ovum is wrapped in a towel and then placed in a small quantity of alcohol and water. This is an excellent method to preserve museum specimens, but it practically ruins every embryo for microscopic study. When an ovum is placed in, say four ounces of strong alcohol, the water of the ovum dilutes the alcohol to a proper strength.

Those physicians who have the proper opportunities should place the specimen as soon as possible, and without opening the ovum, in seventy per cent alcohol, *i. e.*, absolute alcohol reduced by volume to seventy per cent. At the end of a day or two the alcohol is to be renewed, and in this solution the specimen may be preserved indefinitely.

A second convenient method is to place a specimen in quite a large quantity of Müller's fluid, to be changed once or twice during the first few days. The embryo is fully hardened in about a month, and then it is washed in water for a day or

two, after which it is to be preserved in seventy per cent alcohol.

Ten per cent nitric acid is a convenient and a most excellent method. The ovum is to be placed in four or six ounces of a ten per cent solution, and opened while in the fluid, care being taken not to injure the embryo. According to its size (if not over an inch long), it should remain in the acid for from thirty minutes to two hours. At the end of this time it is to be placed in seventy per cent alcohol.

Another excellent method is to harden the embryo in saturated aqueous solution of corrosive sublimate. The specimen is to be treated as in the ten per cent nitric acid, but it is to remain in the sublimate longer. These specimens are then to be preserved in seventy per cent alcohol.

There are many other methods, but if any of the above are employed there will be a sufficient supply of material to aid the study of human embryology. It is really wonderful to see what progress has been made in this study when we consider how difficult it is to obtain good material. Some of the most important discoveries have been made in the careful study of a few well-preserved human embryos, as a glance at the many papers of His and the excellent text-book of Minot will show.

Specimens of human ova are not only of value and interest to the embryologist, but are of great importance to the physician in determining the duration of pregnancy. We can easily see why it is easier to determine the age of a young ovum correctly than to determine the age of the fœtus at full term; in the former the error must be less than a month in order to be overlooked, while in the latter it may exceed this time. Furthermore, in the study of young human ova we may make comparisons with the embryos of other mammals upon which experiment can be made.

Formerly it was quite generally admitted that the age of an embryo is determined by the time of a certain cohabitation. In many cases it was attempted to locate the day exactly. After it had been shown that the ovum is usually extruded from the ovary during menstruation, it was then thought that the egg could be fertilized at any point between the ovary and the uterus. The time required for the ovum to pass through

the Fallopian tube was considered the time in which it was capable of being fertilized.

Our most definite information regarding the fertilization of the mammalian ovum has been obtained from experiments upon the dog, rabbit and guinea-pig. In these animals it is found that the spermatozoa pass through the uterus and tubes in from twelve to twenty-four hours after copulation, and await the ovum in the upper part of the tube. The ovum after leaving the ovary enters the tube before it is fertilized by the spermatozoon, and usually begins to divide before it has reached the middle of the tube. After several days the ovum reaches the uterus, and by this time the egg has divided into many cells, which now begin to arrange themselves in layers to form the blastodermic membranes.

It is possible that the spermatozoa retain their power to fertilize for a very long time, if we can judge by their vitality. Piersol* has recently made experiments upon human spermatozoa and finds that they are motile eight or ten days after removal from the body. From this observation it is fair to assume, as he does, that within the uterus and Fallopian tubes their vitality is still greater. However this may be in man, in the lower mammals the arrangement is such that a large number of spermatozoa await the ovum in the upper part of the tube, and furthermore, coitus in rabbits hastens ovulation (Coste).

The evidence from the above observations is that the ova of many mammals are fertilized in the upper part of the Fallopian tube, and there is every reason to believe that the same is true in man. Tubal and abdominal pregnancies speak for this; in the latter form, the placenta is never attached to the peritoneum but to the mucous membrane of the tube, suggesting that the fertilization took place in the beginning of the tube.

Impregnation is nearly always marked by a cessation of menstruation, and it remains to be shown whether or not the fertilization takes place during the last menstrual period or at the time of the first cessation. The experiments upon lower animals show that fertilization of the ovum takes place soon after the rupture of the Graafian vesicle, and it is fair to assume that the same is true in man. After a Graafian vesicle

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* Piersol: Anatomischer Anzeiger, 1893.

ruptures it is followed by a corpus luteum, but its history is by no means as well known as is generally believed. Our most trustworthy data have been collected by Leopold,* and the more he studied ovaries which had been removed in operations the less definite his conclusions became. We must not lose sight of the fact that the ovaries he removed were to a great extent from women suffering from all kinds of disorders, conditions which no doubt may have complicated his results. In general his conclusion is that a corpus luteum is found in most cases, which from its appearance dates from a menstrual period. During the intermenstrual period he frequently found in addition to a well-formed corpus luteum, a freshly ruptured follicle, indicating that a second and intermenstrual ovulation had taken place. This seems to indicate that ovulation takes place more frequently than menstruation. In other cases in which menstrual periods lapsed the women still continued to ovulate. This is by no means remarkable, for it is known that women often become pregnant before menstruation has reappeared during lactation. Also young girls may become pregnant without ever having menstruated.

From all the observations which have been made the conclusion is that in most cases the corpus luteum begins to form some time during menstruation, but it is extremely difficult to locate the exact date. A few of Leopold's cases which are taken from women just before or during the first few days of menstruation are very important regarding this point. In the table the + indicates the probable time of ovulation.

| Day of Observation after the beginning of Menstruation. | End of Month. | | | | Beginning of Menstruation. | | | |
|---|---|---|---|---|---|---|---|---|
| | 25 | 26 | 27 | 28 | Day 1st. | 2d. | 3d. | 4th. |
| 1 . . . . . | | | + | | | | | |
| 2 . . . . . | | | | | + | | | |
| 3 . . . . . | | | | + | | | | |
| 4 . . . . . | | | | + | | | | |
| 26 . . . . . | | + | | | | | | |

* Leopold: Archiv für Gynaekologie, Bd. xi u. xxi.

In these five cases ovulation took place just before menstruation, and we hope that the near future may add a great many more cases to the table, for the removal of ovaries is by no means a rare operation at the present time.

In spite of our ignorance of the relation of ovulation to menstruation, it is quite certain that there must be one, and that when it is better known it will be possible for us to determine much more accurately the age of embryos and the duration of pregnancy than at the present time. The obstetrician is too well aware that an error of several weeks is often made, and really lays no great stress upon the mistake. This error is not very great for a fœtus at full term, but is very serious when the age of an embryo of the first month is to be determined.

The duration of pregnancy has been studied over and over again, and all kinds of views regarding the time of its beginning have been entertained. In nearly all cases the statistics are not complete, and the results are of little value for us to determine accurately the beginning of pregnancy. Hasler* in his inaugural dissertation has given us trustworthy data of twenty-eight cases in which the menstrual period, date of cohabitation and the birth of the child are given. In addition he gives an extensive discussion of the whole subject in question. I have tabulated twenty-four of his cases from the twenty-eight, excluding the other four because the data are not complete. In all the cases given the cohabitation did not exceed a day, and it is remarkable that in each case the following menstrual period lapsed. The cases were selected by Hasler with great care and bear every cross-examination. In the table I give the average duration of pregnancy when estimated from the beginning of the last menstruation, in the first column, and when estimated from the day of cohabitation, in the second column.

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* Hasler: Inaug.-Diss., Zürich, 1876.

| Time of Copulation. | Number of Cases. | Duration of Pregnancy when estimated from | |
|---|---|---|---|
| | | Beginning of last Menstruation. | Day of Copulation. |
| First week of menstruation. | 9 | 278 days. | 273 |
| Second " " " | 12 | 282 | 272 |
| Third " " " | 0 | No cases. | No cases. |
| Fourth " " " | 3 | 299 | 269 |

The above table contains our most trustworthy cases, and is of much value regarding the duration of pregnancy. Many other cases are scattered through the literature, and at some future date I hope to tabulate most of them.

Leuckart* has given us data of 110 women, each of whom gave birth to a child within ten months after marriage. The cases were all taken from a single village, and for this reason most of them must be trustworthy. In these cases the first cohabitation and the date of the birth of the child are given, but unfortunately the date of the last menstruation is omitted. When the births are tabulated from the date of marriage it is remarkable that the greatest number fall in the 40th and 42d weeks. Stated more accurately, the greatest number fall on the 276th and the 295th days after marriage.

Leuckart believed that these two maxima in the number of births represented the last ovulation before, and the first ovulation after marriage. The 276 days would then represent about 286 days, and the 295 about 285 days.

If we take the three sets of experiments by Leopold, Hasler and Leuckhart we can make them harmonize if we admit that ovulation can take place at any time; it seems as a rule to take place during and immediately after menstruation, and often just before the period. Considering the Graafian vesicle, which is gradually becoming larger and larger, it is fair to assume

* Leuckart: Wagner's Handwörterbuch der Physiologie, Bd. 4.

that its thin wall which is to be ruptured by the hyperæmia of menstruation, can also be ruptured by undue excitement during the intermenstrual period. This is suggested to us in Hasler's cases in which there was but a single cohabitation in unmarried women. The idea is strengthened by Leopold's study of the corpus luteum, and by the fact that coitus hastens ovulation in lower animals.

From the above statement it is quite evident that our information regarding the rupture of the Graafian vesicle, its relation to menstruation and to fertilization of the ovum, needs a most thorough revision. . This cannot possibly be done by one individual alone, and I therefore ask the coöperation of physicians. Each can contribute his part.

Up to the present date our most valuable information regarding the probable time of the fertilization of the ovum has been obtained from the study of a few young human embryos. An error of a few days or weeks would hardly be noticed in a fœtus at full term, but in an embryo two weeks old the same error becomes a matter of great importance. This error has induced embryologists to study the statistics of the obstetricians most carefully.

In order to locate the ovulation from which to compute the age of an embryo, I have tabulated all the young embryos which have been published with a full history. Numbers 2, 3, 4, 6 and 7 are not as complete as they might be, but they are of great value because they fill important gaps. In No. 2 the time between the last menstrual period and the abortion is given roughly as five weeks. Still it is fair to assume that the time must have been between 30 and 40 days. In Nos. 3 and 4 the size of the embryo is not given, but in both cases the ovum is so small that the embryos could not have been over two millimeters long.

From a comparative standpoint we can easily determine the age of human embryos within four weeks. Counting from the last menstrual period, it is very easy to see by the size of the embryo whether or not it is, say three or seven weeks old. The table shows that, by counting in this way, embryos of the same size may differ four weeks in age (see Nos. 6, 14, 16 and 17). In these cases the ages correspond to those of the other cases, if from their time twenty-eight days are subtracted.

# TABLE OF YOUNG EMBRYOS.

| Number. | Observer. | Length of embryo in millimetres. | Beginning of last period. | Last possible cohabitation. | Time of first lapsed period. | Day of abortion. | Time between abortion and Last period. | Time between abortion and First lapsed period. | Probable age of embryo. | Number. |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Mall | .8 | January 25. | ...... | February 22. | March 7. | 41 days. | 13 days. | 13 days. | 1 |
| 2 | Graf Spee | 1.54 | ...... | ...... | ...... | ...... | 5 weeks. | (?) | 7 " (?) | 2 |
| 3 | Reichert | ...... | October 10. | Early November. | November 7. | November 21. | 42 days. | 14 " | 14 " | 3 |
| 4 | Breuss | ...... | × | ...... | × + 28. | × + 38. | 38 " | 10 " | 10 " | 4 |
| 5 | Thomson | 2.1 | × | ...... | × + 28. | × + 42. | 42 " | 14 " | 14 " | 5a |
| 5a | Mall | 2.1 | November 7. | ...... | December 5. | December 18. | 41 " | 13 " | 13 " | 5 |
| 6 | Thomson | 2.5 | May 19. (?) | ...... | ...... | June 1. | 14 " | ...... | 14 " | 6 |
| 7 | His (S R.) | 2.2 | August 15. (?) | ...... | End of September. | October 14-15. | 60 " (?) | 14 " (?) | 14 " | 7 |
| 8 | His (Lg.) | 2.15 | September 10. | ...... | October 8. | October 20. | 40 " | 12 " | 12 " | 8 |
| 9 | Graf Spee | 2.69 | × | ...... | × + 28. | × + 42. | 42 " | 14 " | 14 " (?) | 9 |
| 10 | Janõsik | 3.0 | June 1. | ...... | June 28. | July 13. | 43 " | 15 " | 15 " | 10 |
| 11 | His (BB.) | 3.2 | March 26. | April 4.* | April 23. | May 13-16. | 48 " | 20 " | 20 " | 11 |
| 12 | Ecker | 4. | August 13. | ...... | September 10. | September 27. | 45 " | 17 " | 17 " | 12 |
| 13 | Stubenrauch (K) | 4.3 | April 10. | ...... | May 8. | June 1. | 52 " | 24 " | 24 " | 13 |
| 14 | Wagner | 4.5 | × | ...... | ...... | × + 20. | 20 " | ...... | 20 " | 14 |
| 15 | His (a) | 4.0 | October 4. | ...... | November 1. | November 24. | 51 " | 23 " | 23 " | 15 |
| 16 | His (W) | 5.0 | March 5. | ...... | ...... | March 26. | 21 " | ...... | 21 " | 16 |
| 17 | Hensen | 4.5 | × | ...... | ...... | × + 21. | 21 " | ...... | 21 " | 17 |
| 18 | Stubenrauch (I) | 6.0 | July 1. | July 8. | July 28. | August 14. | 45 " | 17 " | 17 " | 18 |
| 19 | Stubenrauch (II) | 7.0 | April 1. | April 14. | April 28. | May 20. | 51 " | 22 " | 22 " | 19 |
| 20 | Mall | 7.0 | October 6. | ...... | November 3. | November 27. | 52 " | 24 " | 24 " | 20 |
| 21 | His (Stt.) | 7.75 | July 5-8. | July 20.* | August 2-5. | September 1-3. | 57 " | 29 " | 29 " | 21 |
| 22 | Ecker | 10.0 | April 4. | April 15. | May 2. | June 3. | 60 " | 32 " | 32 " | 22 |
| 23 | His ($Br_1$) | 11.0 | April 24. | ...... | May 22. | June 24. | 61 " | 33 " | 33 " | 23 |
| 24 | His ($Br_2$) | 13.6 | October 20. | End of October.* | November 17. | December 22. | 63 " | 35 " | 35 " | 24 |
| 25 | His ($M_2$) | 13.0 | August 7. | ...... | September 4. | October 10. | 64 " | 36 " | 36 " | 25 |
| 26 | His (Lhs) | 17. | May 4. | ...... | June 1. | June 24. | 51 " | ...... | 51 " | 26 |
| 27 | Minot | 22. | January 26. | ...... | February 23. | March 30. | 53 " | ...... | 53 " | 27 |
| 28 | His | 22. | February 21. | ...... | March 21. | April 18. | 56 " | ...... | 56 " | 28 |
| 29 | Mall | 23. | × | ...... | × + 28. | × + 77. | 77 " | 51 " | 51 " | 29 |
| 30 | Minot | 32. | January 4. | ...... | February 1. | March 13. | 68 " | ...... | 68 " | 30 |

* Earliest cohabitation.

1. Mall: Anatomischer Anzeiger, 1893, p. 630.—2. Graf Spee: Verein Schlesw. Holst. Aerzte, Heft 11, Stück 10; His und Braune's Archiv, 1889, p. 159. 3. Reichert: Abhandl. d. Königl. Akad. d. Wissenschaften zu Berlin, 1873, No. 1.—4. Breuss: Wiener med. Wochenschrift, 1877, p. 502.—5. Thomson: Edinburgh Medical and Surgical Journal, 1839, p. 139; and His: A. m. E., I, p. 152.—6. Thomson: Edinburgh Medical and Surgical Journal, 1839, p. 139; and His: A. m. E., I, p. 152.—7. His (S. R.): A. m. E., I, p. 140.—8. His (Lg.): A. m. E., II, pp. 7 and 74.—9. Graf Spee: Verein Schlesw. Holst. Aerzte, Heft 11, Stück 8, 1887.—10. Janõsik: Arch. f. mik. Anat., Bd. 30, pp. 560, 561.—11. His (BB): A. m. E., II, pp. 7, 74.—12. Ecker: His u. Braune's Archiv, 1880, p. 403.—13. Stubenrauch: Inaug. Diss., München, 1889.—14. Wagner: Müller's Archiv, 1835, p. 373.—15. His (a): A. m. E., I, p. 100.—16. His (W): A. m. E., II, pp. 7 and 74.—17. Hensen: His u. Braune's Archiv, 1877, p. 1.—18. Stubenrauch: Inaug. Diss., München, 1889.—19. Stubenrauch: Inaug. Diss., München, 1889.—20. Mall: Journal of Morphology, Vol. 5, p. 459. —21. His (Stt.): A. m. E., II, pp. 8 and 74.—22. Ecker: Icon. Physiol. XXVIII, p. 11.—23. His ($Br_1$): A. m. E., II, pp. 8 and 74.—24. His ($Br_2$): A. m. E., II, pp. 9 and 74. —25. His ($M_2$): A. m. E., II, pp. 9 and 74.—26. His (Lhs.): A. m. E., III, p. 238.—27. Minot: Human Embryology, p. 392.—28. His: A. m. E., III, p. 239.—29. Mall: Not published.—30. Minot: Human Embryology, p. 398.—5a. Embryo from Dr. Ellis, of Elkton, Md.

This seems to indicate that, as a rule, fertilization of the ovum takes place during the ovulation which precedes the first menstruation which has lapsed. After Reichert had shown that menstruation is only a method of clearing out the uterus after an ovulation, and after Leopold had shown that the mucous membrane of the uterus undergoes histological changes before ovulation, it is fair to assume that the latter changes are only preparatory to the reception of the ovum, and that when the unfertilized ovum reaches the uterus, menstruation is only a method of reducing the uterus to its former condition.

It is necessary to compute the age of the embryo from the last menstrual period in only eight of the cases, and it is not probable that just these eight embryos have grown too rapidly. All the rest must have twenty-eight days subtracted from the time in order to make them correspond with the above eight. These are the main reasons for assuming that the fertilization of the egg takes place just before the first menstrual period which lapsed. It may be that a great many fertilizations take place during the last menstrual period, but that when menstruation has once begun, the activity of the uterus destroys the ovum, and that, as a rule, only those are preserved in which menstruation does not follow the last ovulation. At least the embryological evidence indicates that fertilization takes place just before the first lapsed period, and at present embryologists make their specimens correspond to one another by reckoning the ages of most embryos from the last menstrual period minus twenty-eight days.

The table shows, in addition, that in certain pregnancies the first cohabitation followed the last menstrual period. It cannot be that in these cases the ovum of the last period could have been fertilized, for it is quite certain the ovum loses its power of being fertilized shortly after it leaves the Graafian vesicle.

In case No. 11 (B B), the first cohabitation of a newly married woman took place on April 4, say about five days after the last menstrual period; and the woman ceased menstruating at once, probably on account of the fertilization of the ovum which preceded the first lapsed period. If all the cases of newly married women in which there was an early pregnancy were collected it would, no doubt, be shown that in many of

the cases the women did not menstruate at all after marriage. All of Hasler's cases of single cohabitation speak for this.

In several of the cases given in the table, the last cohabitation took place several weeks before the cessation of menstruation, showing that the vitality of the spermatozoa within the female organs lasts for at least a few weeks, or that the last cohabitation was accompanied by an ovulation.

Enough specimens of human ova have been studied and compared with those of lower animals to render it very easy to determine the age of the human from comparative standpoint alone. Thus, for instance, the guinea-pig of two weeks is about as large as the rabbit of the same age. These again are about as large as a dog of three weeks, and all three are of the same stage of development as a human embryo of three and one-half weeks. Then the history of some of the animals closely related to man is now quite well known, and from comparative embryology we can conclude with great certainty whether or not a given ovum is three or four weeks old. In addition to this we have the above table, which cannot be improved much by adding or subtracting a few days from the ages of some of the embryos, as the error cannot be over three days. Therefore we believe that in many cases fertilization of the ovum must take place in the neighborhood of, and usually before some menstrual period. We cannot deny, however, that there may be a difference between the relation of the beginning of pregnancy to menstruation, in first cohabitations, and those which follow later on; in the first, ovulation should be irregular, in the second cases, as regular as it is independently of copulation.

In conclusion, I add a brief history and description of a few young human embryos, and I begin with the youngest which has as yet been cut into serial sections for microscopic study. To be sure, many very young human ova have been seen and the outer forms studied, and the best known of these is Reichert's,* a picture of which is seen in every text-book. Even such a small thing as an unfertilized human ovum has been found in the Fallopian tube,† showing that with industry and

* Reichert: Abhandl. d. Konigl. Akad. d. Wiss., Berlin, 1873.
† Hyrtl: Zeit. f. rat. Med., N. F., IV.

patience "a needle may be found in a haystack." I am under obligations to Dr. Kittredge, of Nashua, New Hampshire, for the above-mentioned specimen. It was quite well preserved when it came into my hands, as it had been placed in a large quantity of sixty per cent alcohol several hours after the abortion. Dr. Kittredge most carefully obtained the history for me, which has borne the most rigid cross-examination in every respect.

"The woman from whom the specimen was obtained is 25 years old, menstruates regularly every four weeks, the periods lasting from four to five days. She gave birth to a child September 19, 1892, and had the first recurrence of menstruation December 19. The second period followed on January 25 and was very profuse; it lasted until February 1. The next period should have begun about February 22, but on account of its lapsing the patient concluded that she was pregnant and called at my office a few days later. I did not examine her, but asked her to remain quiet and await developments, as I thought possible that she might be pregnant. On the evening of March 1 she fell and sprained herself, and during the same night had a scanty flow. The flow recurred each day, and on the seventh of March she passed the ovum. It was kept in a cool moist cloth for twenty hours, and when it came into my hands was at once placed in a large quantity of 60 per cent alcohol."*

The ovum is quite large for its age, having a long diameter of 10 mm. and a short diameter of 7 mm. It is covered with villi only around its greatest circumference, having two spots without villi, as was the case with Reichert's ovum. The villi of the chorion are from 0.5 to 0.7 mm. long and are branched.

Upon opening the chorion it was found that the germinal vesicle was situated just opposite the border of the zone of villi. There was much coagulated albumen around it, which I did not remove and therefore could not obtain good camera drawings. The portion of the chorion to which the vesicle was attached was cut out and stained with alum cochineal and cleared in oil, but even after this treatment it was impossible to obtain any clear picture. The specimen was next imbedded

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* Letter from Dr. Kittredge, April 27, 1893.

in paraffin and cut into sections 10 μ thick. The series proved to be perfect. From the sections a reconstruction was made in wax, and the accompanying figure (Fig. 1) is a sagittal section of it.

FIG. 1.—Sagittal section of the Kittredge embryo. Taken from the reconstruction. Enlarged 33 times. *Ch*, chorion; *AL*, allantois; *x*, position of embryo; *v*, blood-vessels.

The sections and reconstruction show that the embryonic vesicle is attached to the chorion by means of a stem (*Bauchstiel*). The vesicle itself is composed of two layers, between which, at a distance from the stem, there are indications of blood-vessels or a middle embryonic layer. In the immediate neighborhood of the attachment of the vesicle to its stem there is a deep and short invagination of both layers of the vesicle. At first it was somewhat difficult for me to interpret the meaning of the specimen, because there is as yet no decided mark of the embryonic body. The location of the allantois

does, however, give us some clue to the future position of the embryo. It is somewhat complicated on account of the yolk cavity extending into the stem, but I do not think this is serious. I think there is but one rational interpretation of the

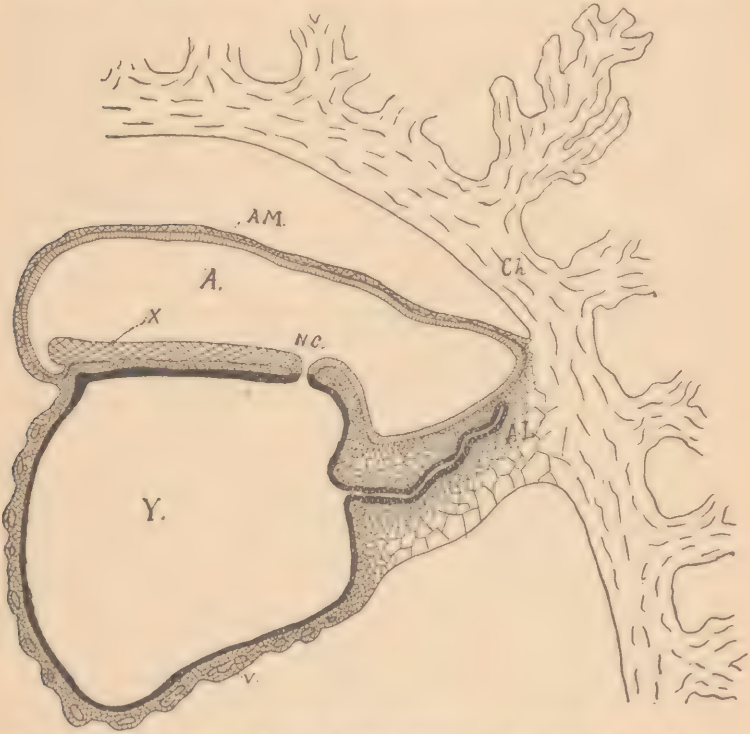


FIG. 2.—Sagittal section of Graf Spee's embryo. *Ch*, chorion; *AM*, amnion; *AL*, allantois; *A*, amniotic cavity; *Y*, yolk cavity or umbilical vesicle; *NC*, neurenteric canal; *X*, embryo: *v*, blood-vessels.

specimen, *i. e.*, it is an apparent inversion of the membranes, as is the case in many of the rodents. The invagination is the cavity of the amnion. It is comparatively easy for us to imagine how this embryo may be changed into one a little older, as for instance that described by Graf Spee. After the opening of the invagination closes, the walls *a* and *a* approach each other and the layers *b* and *b* move down on either side of the invagination. Then the neurenteric canal breaks through. This is practically the state of things as we find them in Graf Spee's embryo.

The accompanying figure (Fig. 2) is from a sketch by Graf Spee,* which he has kindly permitted me to publish. His original publication† does not give the above picture, which is of such great importance in the study of young embryos, and for this reason I add it. As the figure shows, the yolk-sac occupies nearly the whole length of the embryo, and is not much larger than the amniotic cavity. The embryonic medullary plate, *N*, projects slightly forward to form the head-end of the embryo; it is a broad thickened layer of ectoderm, and seen from above is slightly constricted in its middle. Towards the tail-end of the embryo in the middle line there is a communication between the amniotic and yolk cavities, the neurenteric canal; behind this there is a primitive streak. The neurenteric canal or blastopore is the very interesting part in this embryo, because it is the only instance in human embryology in which this canal has been seen. There are many other parts which have been carefully studied in this specimen, but the few mentioned are sufficient to show the great value of it.

When the sagittal sections of the Spee embryo are placed beside that from Dr. Kittredge, we at once obtain suggestions regarding the early formation of the amnion, allantois and yolk vesicle. These parts are by no means formed in the same way in different animals, and up to the present we have had to content ourselves with a theory by His, which has been extensively copied in the various embryologies.

I have drawn the parts I consider homologous with the same kind of lines. A little imagination, aided by some recent work by Selenka‡ on higher mammals is my reason for believing that the invagination in Fig. 1 is converted into the amniotic cavity of Fig. 2.

After the second week a great number of human embryos have been obtained, many of which have been studied carefully by embryologists, especially Professor His. To give an idea of the growth of the external form of embryos, I add a figure taken from His's Atlas.§ The ages of the embryos selected

* Letter from Graf Spee, April 9, 1893.

† Graf Spee: His u. Braune's Archiv, 1889.

‡ Selenka: Studien, Taf. 41, Fig. 6.

§ His: Anatomie mensch. Embryonen. Leipzig, 1880.

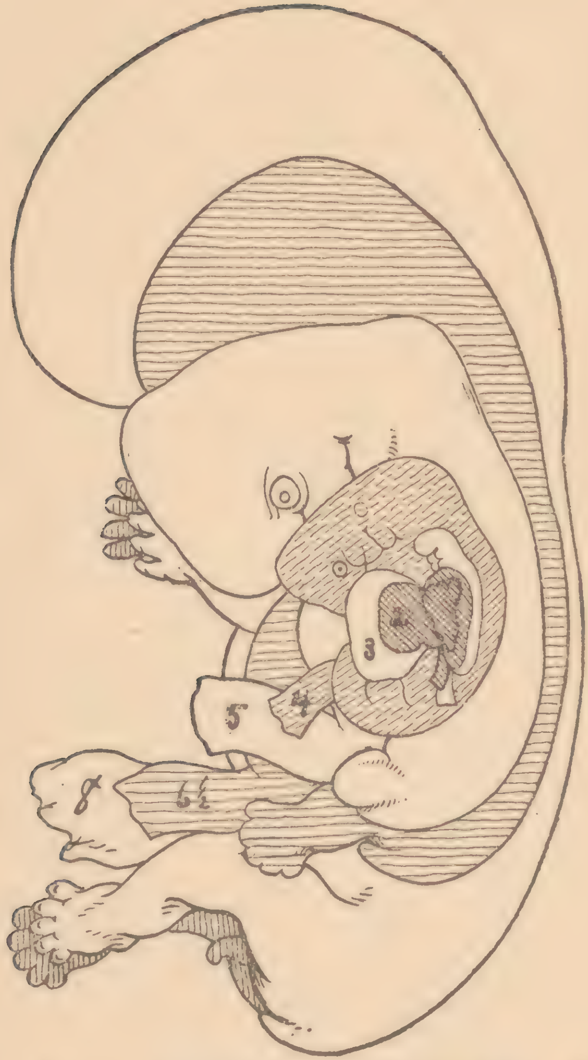


FIG. 3.—Six human embryos taken from His's Standard Chart. Enlarged 5 times. The figures in the cut indicate the age of the embryo in weeks. 2 is His's embryo *SR*; 3, embryo *Lr*; 4, embryo *A*; 5, embryo *C*$^{II}$; 6½, embryo ***XCI***; 8, embryo ***Wt.***

represent from two weeks up to the beginning of the third month. The embryo from which the smallest figure is taken is slightly larger and older than Graf Spee's embryo, and a week later (3) the form of the body is already outlined. During the fourth week the eye, ear, branchial arches and extremities appear, and in the sixth the leg, foot and toes are quite well formed.

The general conclusions formulated by Professor His to determine the age of human embryos are, when slightly modified, as follows:

1. The beginning of development is the time of impregnation, *i. e.*, at that moment when the spermatozoon enters the ovum.

2. The time the egg leaves the ovary is marked by menstruation, but it is not necessary for the Graafian vesicle to rupture during menstruation; it may take place immediately before, during, or after the hemorrhage.

3. The egg is not capable of being fertilized at any point from the ovary to the uterus, but only shortly after it has left the ovary; as a rule, as it is entering the Fallopian tube.

4. The spermatozoa which have entered the female sexual organs must await the ovum in the upper part of the Fallopian tube, and can retain their vitality here several days, or possibly several weeks. The time of cohabitation is, therefore, not directly related to the age of the embryo.

5. The age of many embryos is to be estimated from the beginning of the first menstrual period which has lapsed, although it is possible to have a menstruation after fertilization of the ovum.

6. The age of an embryo can be expressed by the following formulas: $A = X - M$ or $A = X - M - 28$, in which $X$ is the date of the abortion and $M$ the beginning of the last period. The second formula is for cases in which it is necessary to count from the first lapsed period.

There is no reason why the gynecologist should not add his share in determining the age of embryos. Any physician can add greatly to the subject if he will record all cases in his practice after the plan of Dr. Kittredge's letter. It is not necessary for him to confine himself to young embryos alone.

but he might also include fœtuses at full term; especially those of newly married women will be valuable. Moreover, if the young specimens are carefully preserved, he will do a great work hand in hand with the embryologist.

To facilitate the arrangement of data which may be obtained, I append two tables with a single case in each.

THE HISTORY OF AN EMBRYO.

| Beginning of last menstrual period. | Duration of period. | Frequency of periods. | Date of abortion. | Dimensions of embryo. | Remarks. |
|---|---|---|---|---|---|
| Oct. 6 | 4 days | 28 days | Nov. 27 | Ovum not opened. | Hardened in alcohol 3 hours after abortion. |

HISTORY OF A CHILD BORN WITHIN TEN MONTHS AFTER MARRIAGE.

| Beginning of last period before marriage. | Duration of period. | Frequency of periods. | Date of marriage. | Dates of periods after marriage. | Duration of last period. | Date of birth of child. | Remarks. |
|---|---|---|---|---|---|---|---|
| Dec. 10 | 5 days | 28 days | Jan. 1 | Jan. 7 | 3 days | Oct. 7 | Boy, very large. |

If there is more than one period after marriage, the date and duration of each should be given.